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# A Pilot Study of the Relation of Selected Nutritional Factors to Skeletal Age of Galactosemic Children

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LOMA LINDA UNIVERSITY
SCHOOL OF GRADUATE STUDIES

# A Pilot Study of the Relation of Selected Nutritional Factors to Skeletal Age of Galactosemic Children

by

Jessie Merle Harper

A Thesis in Partial Fulfillment
of the Requirements for the Degree
Master of Science in the Field of Nutrition

June 1964

I certify that I have read this thesis and that in my opinion it is fully adequate, in scope and quality, as a thesis for the degree of Master of Science.

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TABLE OF CONTENTS

## LIST OF TABLES

## LIST OF FIGURES

# CHAPTER I

## THE PROBLEM AND DEFINITIONS OF TERMS USED

The research which has been done in the past has accomplished much in eliminating many of the symptoms of galactosemia. However, even with treatment, certain manifestations of the disease have not been adequately controlled, for unexplained reasons. Skeletal age in some of the galactosemic children has not seemed to consistently follow the normal pattern as established by Greulich and Pyle. (36) Whether this bone retardation could be significant in relationship to the disease or its dietary management has not been investigated.

### I. THE PROBLEM

Statement of the Problem. It was the purpose of this study (1) to compile data from the medical records of galactosemic children in such a way that the dietary intake of calories, protein, calcium and vitamin D would be easily visualized as compared with the Recommended Daily Dietary Allowances of the Food and Nutrition Board of the National Research Council, and (2) to ascertain if there is a relationship between this dietary data and the skeletal age of the child.

Importance of the Study. Much of the work in the past on the disease galactosemia has been done to aid in diagnostic procedures. Dietary control, if followed through, has not proved a difficult task. However, even with adequate dietary control, there were many problems left unsolved which have concerned those who have worked with the disease. One of these problems was the frequent occurrence (nine out of seventeen in this study) of retarded bone growth in the galactosemic child. By carefully recording a nutritional history of the dietary intake over a period of years, it would be possible to determine if there might be

some nutritional cause for the retarded bone growth. If this could be proven true, dietary regimes could be used as a therapeutic measure to control this problem

Limitations of the Study. To conduct a study whereby the existing data from medical records must be analyzed presented several problems which will be discussed here.

One of the major problems was that the data were collected from many sources, i. e. clinical laboratory, radiology, examining physician and nutritional reports. The report from one of these sources frequently did not coincide in time with the report from another one of these sources. For example, a child might have had a physical examination at one time during the year and be scheduled for a skeletal age study to be done at a later time.

Another problem in conducting a study where the human element was concerned was the emotional feelings of the individuals. Since the study dealt exclusively with children, the parent's attitudes and parental feelings had to be considered. One mother refused to have an X-ray taken of her child's wrist for fear of leukemia. She had had a friend who had lost a child from this disease and the child had been X-rayed several times. The friend had become convinced that the X-rays were a contributing factor in the disease, and had passed her fears on to this mother.

Insufficient data were another limitation throughout the entire study. The medical records proved to have insufficient dietary data for any valid conclusions so that more information had to be obtained. This was done by mailing out nutritional history forms to each family involved in the study. At the end of the survey, it was found that of the 102 forms mailed out, less than half had returned.

Another limitation was in calculating the correct amount of calcium in vitamin and mineral preparations. The pharmaceutical compan-

ies who made calcium tablets used by the children in the study were contacted. It was found that the calcium listed on the labels of various products usually was in terms of the calcium salt rather than the actual amount of calcium supplied in the tablet.

## II. DEFINITIONS OF TERMS USED

Casilan. A calcium salt of casein, containing approximately 90% protein, usually in combination with coconut oil, arachis oil and sucrose, and used as a milk substitute formula. (4) (19)

Nutramigen. A synthetic "milk" manufactured by Mead-Johnson in which the formula is made from casein enzymatically hydrolyzed to reduce allergenicity, and containing dextri-maltose, amigen, corn oil, arrowroot starch, vitamins, calcium gluconate and other mineral substances. (4)

Wanderlac. A soybean preparation manufactured by A. Wander Ltd. of London, England. (86)

## CHAPTER II

## REVIEW OF THE LITERATURE

In the past few years there has been great emphasis in research work on the inborn errors of metabolism. Much has been published regarding the diagnosis and treatment of galactosemia; however, only a brief summary of the work done on this medical problem will be presented here.

### I. Brief History of Research

Galactosemia, one of several diseases classified as "inborn errors of metabolism", is characterized by the inability of the organism to properly utilize galactose. Von Reuss in 1908 gave the original description of galactosemia, but it was not until 1917 that Goppert attached a genetic significance to the disease by reporting a case in a child four years old who had three siblings with suggestive histories of galactosemia. (8) (23)

In 1935, Mason and Turner studied the case of a male Negro infant whose symptoms of galactosuria, malnutrition, hepatosplenomegaly and impaired hepatic and renal function strongly suggested galactosemia. When he was observed years later, cataracts had developed. The follow-up in 1951 when the patient was 18 years old indicated an increased galactose tolerance. (8) At the age of 24, in 1957, this same patient appeared to be the oldest living person in whom the diagnosis of galactosemia had been established. At that time the uncontrolled ingestion of milk caused no overt clinical manifestations. (8) (17)

Dietary treatment and its significance began to attract the attention of researchers in the nineteen-forties. Norman and Fashena, in 1943, described a case in which a galactose-free diet resulted in the disappearance of symptoms and the return to normal of liver function. (8)

Several investigators between the years of 1946 and 1948 demonstrated the clearing of cataracts by using dietary restrictions of lactose. Then in 1950, liver biopsy studies enabled Bell and co-workers to describe the early fibrotic changes in the liver cells themselves. Townsend, with his associates, emphasizing the complication of mental retardation, presented Mason's original patient as a study, showing the patient's intelligence quotient was in the retarded range. (8) (17)

## II. Etiology and Genetics

Enzymatic defect. Researchers have generally agreed that the metabolism of the body is regulated by an intricate system of enzymes, the synthesis of which is under genetic control. Whenever there is a defect in this control, the result may be a defect in the formation of one or more specific enzymes, and this may mead to an inborn error of metabolism. (5) (12) (18) (23) (32) (72) Schwarz made the first important observation which led the way in finding the underlying lesion responsible for the enzymatic defect of galactosemia. He showed that normal red cells were able to metabolize galactose but that the cells of the galactosemic patient were unable to do this. Schwarz, with his co-workers, noted that the erythrocytes of patients with galactosemia accumulated galactose-1-phosphate after ingesting milk or galactose. (5) This suggested that there was a block in the conversion of galactose-1-phosphate to glucose-1-phosphate which would involve the enzyme galactose-1-phosphate uridyl transferase. The further studies of Schwarz demonstrated that normal red blood cells contain this enzyme whereas the red blood cells of patients with galactosemia do not. The presence or absence of this enzyme in the blood was determined quite easily. (3) (50) (58) (60) (87) Anderson and co-workers found that human erythrocytes normally contain a considerable amount of galactose-1-phosphate uridyl transferase, but in human congenital galactosemia, the enzyme was missing in the hemolysate or was present in amounts less than five per cent of the normal. These workers discovered that an enzymatic assay could then be used to diagnose cases of congenital galactosemia. (3) Bretthauer and Hansen modified the original transferase assay to include the measurement of the intermediate enzyme activity. (9) The test proved to be simple enough for routine clinical use. (23)

Genetic Aspects. Bonner has stated, "By definition we know that genes are the smallest units of inheritance and are arranged in linear fashion on a gross cytologic unit, the chromosome....." (18) Genes are composed of nucleoprotein and have the ability to undergo self-duplication. If the gene shows alteration, this mutated gene then subsequently will duplicate itself. Only after a gene has changed and therefore has a concomitant loss of function will it be able to be recognized. It has been assumed that all enzymes are under the control of genes and it has been generally accepted that the absence and/or presence of enzymes and their function is determined genetically. (18) (44) (103) Whether one or several genes could be responsible for one enzymatic reaction was not determined prior to 1955. (45)

In 1923 Garrod developed the theory of congenital absence of enzymes leading to a block in the metabolic pathway. If the metabolic pathway were traced in its individual stages it would be possible to identify the faulty link. This theory of metabolic chain reactions opened up a new line of research in both genetics and biochemistry. (41) (45) The criteria as established by Garrod to determine if a metabolic disorder could be termed an "inborn error of metabolism" were: (1) that the metabolic aberration is congenital, (2) is present throughout life, and (3) is hereditary. Galactosemia has fulfilled Garrod's criteria. (12)

Childs and associates have found from microbial genetics that wherever there is evidence of a change in enzymatic activity with an accumulation of some precursor substance or a deficit of some other protein substance that, supposedly, a mutant gene was at work. A mutant gene, therefore, is probably responsible for galactosemia. (12) (103)

The frequent occurrence of galactosemia in siblings and among the children of consanguineous matings plus its equal distribution in both

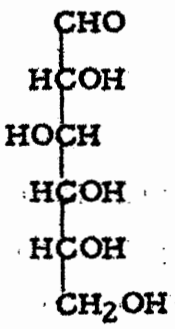
sexes has suggested that galactosemia probably was transmitted by a single autosomal recessive gene. In a situation such as this, it would be expected that the disease would occur only in persons who have received two of the abnormal genes - one from each parent. Hsia and his co-workers have found that the individual who is heterozygous for the condition will usually be free of the clinical symptoms. (52) Donnell, with his associates, has conducted a study on thirteen families known to have at least one member with galactosemia. This study supported the theory that galactosemia is transmitted by simple Mendelian inheritance, that it showed no predilection for either sex and is distributed equally between the sexes; therefore, galactosemia is not sex-linked. (23) (24)

A chance discovery of an adult who was proven to have galactosemia by the galactose tolerance test and by the determination of galactose-1-phosphate uridyl transferase level in his blood gave Hugh-Jones and his co-workers evidence that the disease is transmitted by a Mendelian autosomal recessive gene. This discovery also gave opportunity to show how enzyme studies in a family can be used as diagnostic procedures to detect heterozygotes and to show that these individuals might be relatively free of clinical symptoms. The individual observed by these investigators had affected grandchildren. From previous studies it would have been expected that he would have two abnormal genes for galactosemia and that he would have transmitted to each of his children one of the abnormal genes. Enzyme levels were done on his family, and his six children were shown to be heterozygous carriers of the condition. One of his children had married another unrelated heterozygous carrier and they had two affected children in their family of four. (50)

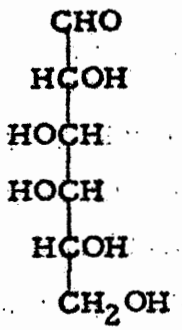
III. Biochemistry.

Galactose metabolism. Galactose is a six carbon sugar (hexose)

similar to glucose in structure except for the H and Oh groups about the fourth carbon. The following diagram illustrates this difference:

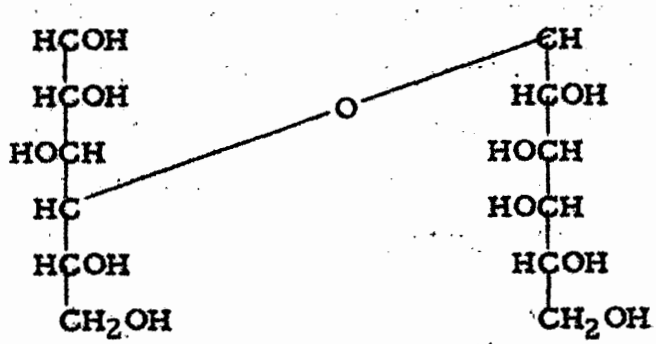



D-glucose




D-galactose

Galactose is an important source of energy in the first few years of life; however, it is not found in nature as such, but in the form of lactose, a disaccharide. Lactose is found to the extent of about 5% in the milk of cows and about 7% in the milk of humans and is apparently solely of mammalian origin. Its structure is as follows:




D-glucose portion D-galactose portion

Upon hydrolysis it yields an equimolar mixture of galactose and glucose. This hydrolysis takes place in the intestines and after galactose is absorbed from the intestinal tract, it is transported to the liver where it is converted to a great degree into glycogen. As the occasion demands, this stored glycogen may be converted to glucose for energy needs. Glucose may be synthesized into glycogen or broken down to many intermediate compounds and oxidized to $CO_2$ and $H_2O$. The latter supplies the body with heat and energy required for normal physiological processes. Glyco-

gen is the storage medium for future energy use in the event there is insufficient flow of glucose into the cells. It is in the form of glucose that galactose is utilized for energy. Galactose is absorbed as quickly as glucose but is metabolized less rapidly and less completely. Unlike glucose, galactose cannot be directly utilized by the brain and will not relieve symptoms of hypoglycemia. (8) (17) (42)

Normally, galactose, together with glucose, is released by the hydrolysis of lactose and enters the liver where phosphorylation takes place. (41) Five enzymatic reactions are important in this galactose-to-glucose interconversion. In the liver the galactose first combines with phosphate from adenosine triphosphoric acid, under the influence of the enzyme galactokinase. (54) Figure 1, page 11 best illustrates this interconversion. (53) (58) (100)

Alternate Pathway. In galactosemia the enzyme galactose-1-phosphate uridyl transferase is absent and this results in the accumulation of galactose-1-phosphate. The absence of this enzyme prevents the conversion of galactose-1-phosphate to uridine diphosphate galactose, where it can be epimerized to glucose and then oxidized to carbon dioxide. However, the enzyme uridine diphosphogalactose pyrophosphorylase is present, and it is believed that this mades possible an alternate pathway for both the utilization of galactose-1-phosphate and the synthesis of uridine diphosphate galactose. There is evidence available for the existence of this enzyme in mammalian liver. Through a studies on rat, pigeon and human liver, this has been proven true. The livers of these animals were examined and were found to contain enzymatic activity. The enzyme, uridine diphosphoglucose pyrophosphorylase, has been found in significant amounts only in the liver, where its activity is approximately 1/6th that of galactose-1-phosphate uridyl transferase. (23) (60)

In the conversion of uridine diphosphogalactose to uridine diphosphoglucose, a specific epimerase is required. Since this reaction is

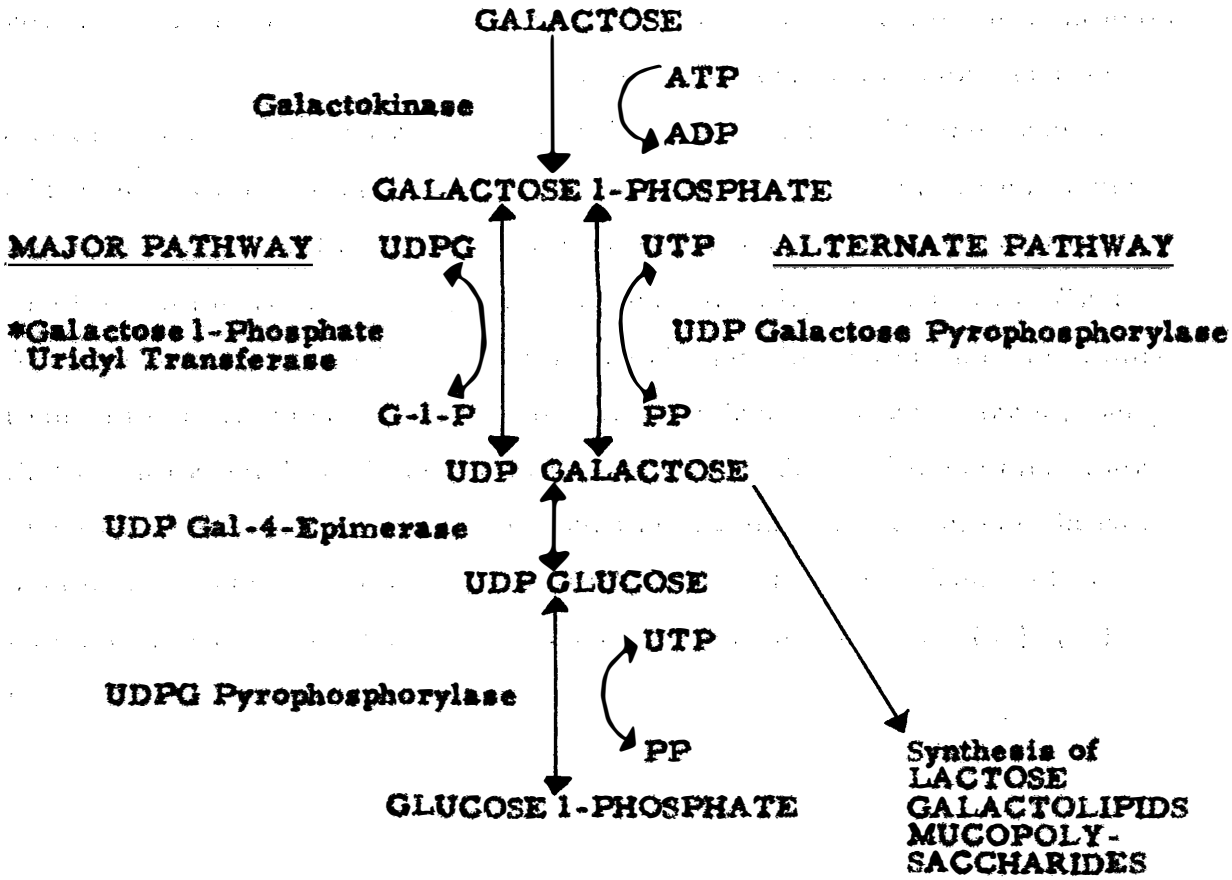



FIGURE I

METABOLISM OF GALACTOSE

A schematic representation of the metabolism of galactose. The following abbreviations are used: ATP, adenosine triphosphate,; ADP, adenosine diphosphate; G 1-P, glucose 1-phosphate; PP, pyrophosphate, UDP uridine diphosphate; UDPG, uridine diphosphoglucose; UDP Gal, uridine diphosphogalactose; UTP, uridine triphosphate.

* Represents the enzyme which is absent in galactosemia.

reversible, it may be a source of endogenous galactose for the synthesis of essential galactose-containing compounds such as the cerebrosides and the mucopolysaccharides. One of the most vital of these groups of tissues is the galactolipids known as the cerebrosides, which occur most abundantly in the myelin sheaths of nerves. Cerebrosides are involved in the rapid myelinization which normally occurs in the first few weeks or months of life. Current evidence indicates that the galactose in these tissues is not derived directly from dietary sources, but that a major portion of the galactose is derived from glucose and other procursors. It has been implied that the patient with galactosemia can synthesize essential galactose even when on a galactose-free diet because of the reversibility of the process mentioned above. (23) (38) (58)

## IV. Symptoms, Laboratory Findings and Treatment.

Symptoms. The symptoms of galactosemia, as stated by Donnell and co-workers, appear early in infancy, occurring usually within the first weeks of life. Some of these symptoms include: failure to gain weight, retardation of development, enlargement of the liver and spleen, galactosuria, excretion of albumin in the urine, often osteoporosis, the formation of cataracts, and increased susceptibility to infection. (6) (23) (27) (58) The infant may appear normal at birth, but as milk is included in the diet, the symptoms begin to manifest themselves. One of the earliest signs of galactosemia is jaundice, which occurs from 4 to 10 days of life and is prolonged past the usual period of physiologic icterus. (22) Ascites, vomiting and diarrhea accompany the other findings in many of the cases. Lethargy, hypotonia and anemia are frequent findings also. (53) If the clinical manifestations appear very mild, the diagnosis may be overlooked for weeks or even for months. Nevertheless, even mild symptoms, if accompanied by an intolerance to milk should suggest the clinical diagnosis of galactosemia. (23) Bain and associates have found that a failure to diagnose galactosemia may be caused by several reasons. Some of these are: (1) failure to obtain the urine specimen while the infant is on a milk feeding, (2) failure to consider all atypical cases of jaundice in the neonatal period, and (3) failure to consider all dystrophic and marasmic infants in diagnostic procedure. (5) Donnell and his co-workers have urged that whenever there is any suggestion of galactosemia, that definite laboratory tests be made before dismissing the diagnosis. (21) (23)

Laboratory Findings. Blood. Schwarz and his associates have concluded that the safest method of recognizing the abnormality of galactosemia soon after birth is to test cord blood. The method, as explained by them, is based on the observation that the incubation of

galactosemic erythrocytes with galactose will lead to the accumulation of galactose-1-phosphate in the cells. The margin is wide between the behavior of normal and galactosemic erythrocytes, thus assuring a firm diagnosis. On the basis of this test, the diagnosis of galactosemia can be made by the third day of life, even with no clinical symptoms. The infant can then be put on a milk-free diet. For all practical purposes the test cannot be applied to all newborn infants, but could be used on all those who have a family history suggestive of the disease. (78) (86)

The chromatographic method of qualitatively identifying galactose in the blood is the most reliable method, Donnell and his co-workers have found. It is a highly specific test and can be used as a diagnostic aid. (5) (23) (72)

The galactose tolerance test can be used as a valuable diagnostic aid, also, but it has a tendency to induce hypoglycemia and hypokalemia. Because of this it may constitute a danger to some patients. Donnell and his associates have felt that if there are not available means for measuring the enzyme itself, then this test may be used for a verification of diagnosis. (23)

In patients suffering from galactosemia, there will be an elevated blood galactose level , reduced galactose tolerance and a deficiency of galactose-1-phosphate uridyl transferase in the erythrocytes and other tissues. Determining the absence of this enzyme in the erythrocytes of persons with galactosemia is a relatively simple diagnostic test. It has been shown to be specific since the erythrocytes of normal persons will contain this enzyme while those who have the disease will not. A modification of this test allows for the detection of the asymptomatic heterozygote. (5) (23) (48) (58)

Urine. Finding a reducing substance in the urine is relatively easy, but identifying it presents a more complex problem. Lockhart

and co-workers have found that the usual test for reducing sugars does not differentiate between galactose and other reducing substances which might be in the urine, such as glucose, fructose, pentose and even lactose. Bray and associates report that a reducing substance may vary in amount from day to day, depending on the diet. Figure 2 outlines the different methods of identifying a reducing substance in the urine. (79) A positive mucic acid test will determine the sugar to be either lactose or galactose. Then a Rubner test may be used to eliminate lactose. A Tollen's phloroglucinal reaction and a preparation of galactose osazone will confirm galactosuria. This osazone test works well with pure sugars, but crystal formation is influenced by other substances in the urine. The various color tests are not specific enough either, especially if the sugar is present in only small amounts. (8) Therefore, paper chromatography has proven to be a definite method of identifying galactose in the urine as evidenced by the work of Lockhart and co-workers. (72)

Another finding in the urine of infants with galactosemia is proteinuria and aminoaciduria. Donnell and his co-workers propose that the proteinuria is probably caused by the toxic effect on the kidney of the accumulated metabolites of galactose. These same investigators have also demonstrated that the protein disappears from the urine within 4 to 6 days after milk is removed from the diet. (5) (23) (69)

Aminoaciduria has occurred in the urine of untreated infants with galactosemia. The occurrence of aminoaciduria in a condition such as galactosemia would, at first, suggest that the aminoaciduria had occurred as a result of a rise of plasma level due to impaired deamination by the liver. However, from the work of many investigators, it has been shown that the pattern of amino acid excretion does not resemble that of the overflow variety of hepatic origin. It has been

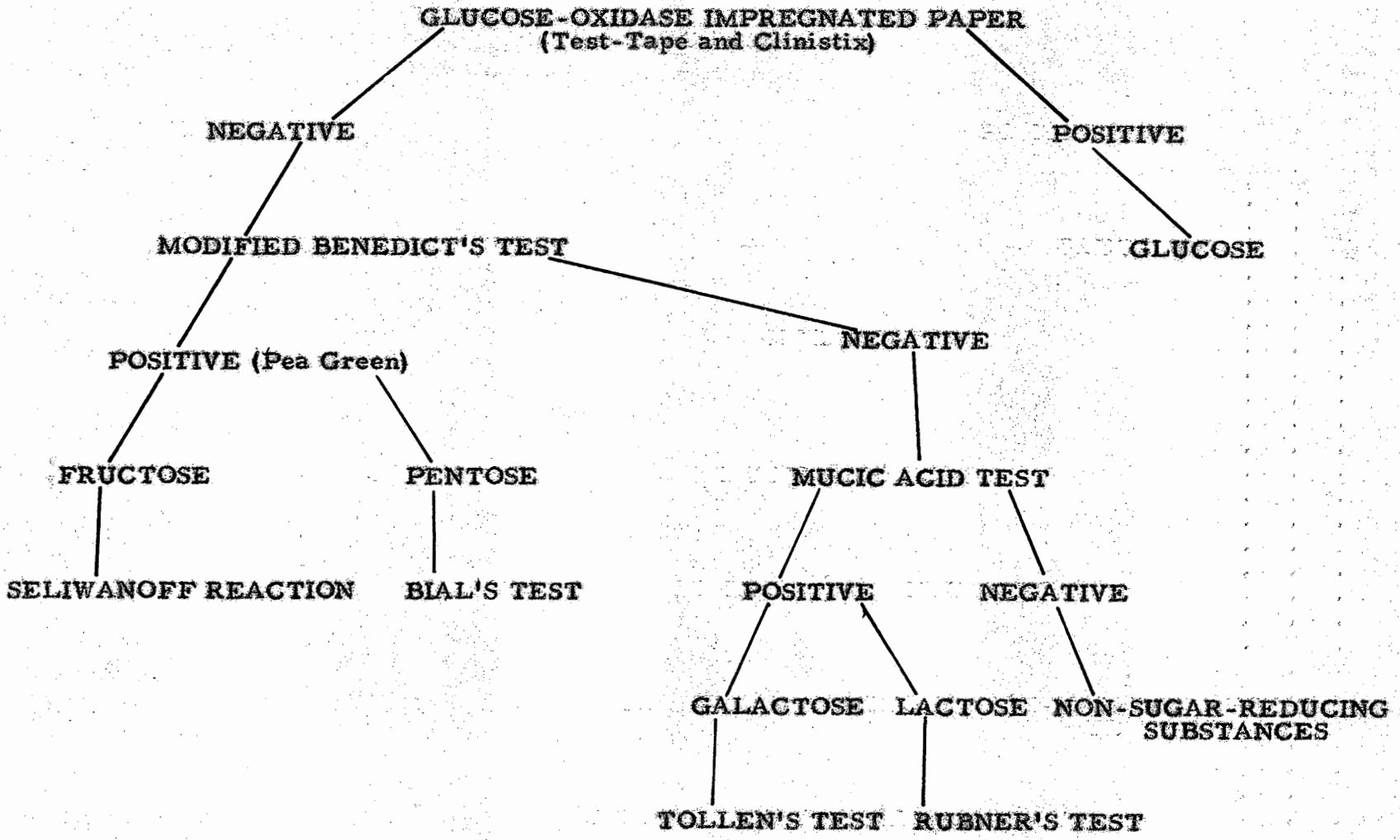



FIGURE 2

IDENTIFICATION OF URINARY GALACTOSE

Schema for the differentiation of urinary reducing substances as detected by routine Benedict's test or by Clinitest. Modified from Page and Culver. (79)

found that the mechanism is a renal one, probably due to diminished tubular reabsorption of amino acids by the kidneys. (20) (23) (43) (50) (57) (66) Plasma concentration of amino acids remain normal in galactosemia and this fact has indicated that the aminoaciduria must be due to impaired renal absorption rather than to a flooding of the kidney. (50)

Many investigators have studied the pattern of amino acids excreted in the urine of patients with galactosemia and the pattern appears to be essentially similar in all cases, with a predominance of the neutral, simple aliphatic chain type. This would include amino acids such as glycine, alanine, threonine, serine, glutamine and valine. In addition to these, several other amino acids have been detected in the urine. Some of these are: phenylalanine, lysine, cystine, glutamic, methyl histidine, tyrosine, and iso-butyric acids. (57) (69)

Guest has postulated that the excretion of the essential amino acids, some in considerable quantities, may have significance in the development of symptoms of nutritional deficiencies in galactosemia whenever it is left uncontrolled. (37) Donnell and his co-workers feel that aminoaciduria presents a much more sensitive measure of galactose intake than either galactosuria and/or proteinuria. They reason that if aminoaciduria persists throughout treatment, it will suggest imcomplete dietary restriction. (21) (23)

Liver Findings. The liver has been consistently affected in galactosemia, but the usual tests of hepatic function are not diagnostic in this instance. Donnell and his associates have found that even in severe liver damage, cephalin-cholesterol flocculation and tymol turbidity tests may be normal. In another study, these same workers have found through autopsy many of the pathologic manifestations of liver function disorders. For example, these studies have shown many

hepatic cells distended by a single large lipid vacuole, focal cellular necrosis and early fibrotic changes. (8) (21) (23) (24) (26) (56) (62) (88) (96)

Treatment. Dietary Treatment. Hsia and O'Flynn have stated that, "the design of the diet free from lactose in the very young baby is not easy". (48) (52) However, it is known that diet excluding galactose will produce a reversal and complete clearance of most of the symptoms of galactosemia.

Holzel and other workers introduced a lactose-free diet based upon a milk-free diet as devised by Moll and Stransky years before. (41) (45) Moll's formula consisted of rice, water, eggs, glucose, salt and bicarbonate of soda. (57) (63) To this Holzel and his co-workers added margarine. It proved an extremely high carbohydrate food and caused some gastro-intestinal disturbances in the very young. It was important to dilute this mixture and also to supplement it with orange juice and calcium. (44) (45) (46) (51) (52)

In their studies, Cox and Pugh used "Casilan", a milk protein formula. To this they added coconut oil, arachis oil, sucrose and water. Plus vitamin supplementation, this mixture required the addition of potassium, sodium and iron salts. It did have an adequate amount of calcium and phosphorus but also contained about 12 mg. of lactose in each ounce of feeding. (4) (19) (63)

In the past, Holzel and his workers have pleaded for a diet completely free of galactose. Soya milk preparations do include small traces of galactose-containing sugars, such as stachyose, a tetrasaccharide; however, Koch and his associates have shown that these substances do not liberate galactose in the body. Many investigators have used soya milk preparations with success. (23) (37) (38) (44) (45) (51) (52) (53) (63) (64) There have also been cases where the

use of a soya bean preparation, such as Wanderlac, did not produce satisfactory results, but whenever the child was placed on Nutramigen, there was an immediate response of weight gain with steady improvement. (22) (67) (87)

Nutramigen is a casein hydrolysate and has been used successfully by several investigators. (23) (47) This contains 0.09% galactose. However, most researchers in the United States have agreed that the amount of galactose (or lactose) found in the casein hydrolysate is insufficient to have any adverse affect on either growth or mental development. (23) (66)

Orotic Acid Treatment. Tada and his fellow workers have recently discovered a beneficial effect of orotic acid therapy in galactose metabolism. Two patients with galactosemia were given oral administration of orotic acid for two weeks. Throughout the experiment, a mixed amount of cow's milk was given every day. Before and during the treatment, galactose content in the urine was determined. The urinary excretion of galactose in both cases was felt to be definitely diminished after oral administration of orotic acid. Along with this, there was a steady improvement of symptoms and clinical findings of both patients. This study may offer a new approach to the treatment of galactosemia, but, at present, much more research will need to be done before any conclusions as to its benefit may be drawn. (92)

V. Maturation and the Skeletal Age.

Maturation. Maturation as defined by Todd means, simply, progressive growing. This term was illustrated by the growing up, growing older and growing old phase of human life. This type of progressive growing has shown evidence of being shared by all humanity, regardless of size and experience. Whenever there is disturbance in this progress, it may show itself only vaguely in stunted growth, or it may even be in the form of excessive stature. (94)

As Todd explained, the maturation process manifests itself in every part of the skeleton, but it is in the transformation of fibrous tissue and cartilage into bone that the most easily identifiable criteria present themselves. A reliable and precise method for determining the various stages of maturation would be an extremely useful tool. Such a tool was found in the X-ray study of the hand and wrist. The roentgenographic technique provided a ready, easily applicable and non-injurious method of determining general bodily development. (36) (94)

Skeletal Age. It has become customary to express the skeletal status of a child in terms of his skeletal age. Used in this respect, the skeletal age corresponds to the chronological age at which the children on whom the standards were based usually attained that same degree of skeletal development. Thus, this measuring tool made it possible to relate the child's skeletal status to his chronological age. Along with other data on which an appraisel is based, the X-ray of the hand and wrist provides valuable information about that particular child which could not be obtained in any other way. (36) (94)

## CHAPTER III

## METHODS OF PROCEDURES

The methods of procedure are discussed in three general classifications:

1. Selection of subjects.
2. Collecting and Recording the data.
3. Analysis of data.

Selection of subjects. Seventeen of the twenty-five children with galactosemia who are regularly seen at the Child Development Clinic of the Children's Hospital of Los Angeles were selected for this study. These children were selected on the basis of the parent's ability and willingness to cooperate.

At the beginning of the study there was a wide range in ages from an infant three months old to a child twelve years old. There was also a variance in the ages when dietary measures were instituted. Five were started on dietary treatment at birth due to an elevated galactose 1-phosphate uridyl transferase level in the cord blood. The latest age at which the galactose-free diet was begun was five years and nine months. The majority of the children were started on a diet within the first few weeks of life. See Appendix 1, page 58 for an outline of this galactose-free diet.

Of the seventeen selected, there were three pairs of siblings. In each pair, there was a male and a female.

Collecting and Recording the data. The medical records of seventeen children with galactosemia were studied for previous data pertinent to their growth and development. The data which were especially emphasized were: nutritional information and skeletal radiological reports.

The galactosemic children made visits to the Child Development Clinic periodically, depending upon the age of the child, the blood level

of galactose 1-phosphate and the child's general well-being. These visits vary from once every three months to once a year. The children who have been under dietary treatment since birth are not seen as frequently as the children who were diagnosed later and who had been extremely ill before the diagnosis was confirmed. At each visit, the child is weighed and measured, and the parent is interviewed by the nutritionist as to the child's dietary pattern.

After the data from the medical charts were recorded, it was discovered that sufficient dietary evidence was lacking to form any valid conclusions. It might be well to note here that, in the past, the importance of continuous diet therapy with a galactose-free diet was not clear due to a lack of scientific evidence regarding the prognosis. (67) Therefore, a program was instituted whereby once a month a three-day nutritional history form was mailed to the parents for recording the dietary pattern of each child. Enclosed within each letter was a self-addressed envelope in which the forms could be mailed to the nutritionist. The first set of forms was postmarked the last week in August, 1963, and the last set of forms was mailed the first week in February, 1964. A sample of this form is found in Appendix 2, page 59.

Analysis of data. When the forms were returned, the three-day dietary pattern was analyzed for its content of calories, protein, calcium and vitamin D, taking into consideration all supplementary vitamin and calcium preparations which may have been included in the diet. From this data a three-day mean value was derived, which was used as a representation of the nutritional status for each month of the study.

Out of the seventeen children selected originally for the study, five were eliminated because of insufficient returns of the nutritional history forms. It was not possible to determine the reason for the failure in returning the forms.

Once the mean value of a three-day nutritional intake of calories, protein, calcium and vitamin D was determined, it was compared with the Recommended Dietary Allowances as revised in 1963. Any nutritional data computed previously on the medical records were also revised to agree with the newly established recommended allowances.

## CHAPTER IV

## INDIVIDUAL CASE PRESENTATIONS

In order to better understand the results of this study, the individual cases are presented, with the object of giving more background information. Much of the data could not be included in graph form because of the wide variance in the time at which the data were received.

### I. CASE A

This two year old female was born in 1962, diagnosed at the age of two weeks and immediately placed on Nutramigen. She required intravenous feedings prior to this because of vomiting. Ninety-six hours after she was born, her blood was exchanged because of a bilirubin of 20 mg. due to impaired liver function.

She appeared to develop well and at six months had a good appetite. She took Nutramigen well and also her supplementary feedings were accepted without difficulty. She teethed at four months and by six months, she had two lower teeth of good quality. By nine months of age, she had two upper teeth and three lower teeth. She was walking by twelve months.

Two bone age studies were done: (1) one at three months of age which showed a reading less than her chronological age; and (2) the other at eighteen months of age which was within normal range.

This child has two brothers, one older and one born since the study began. Her case is illustrated by Figure 3, page 25.

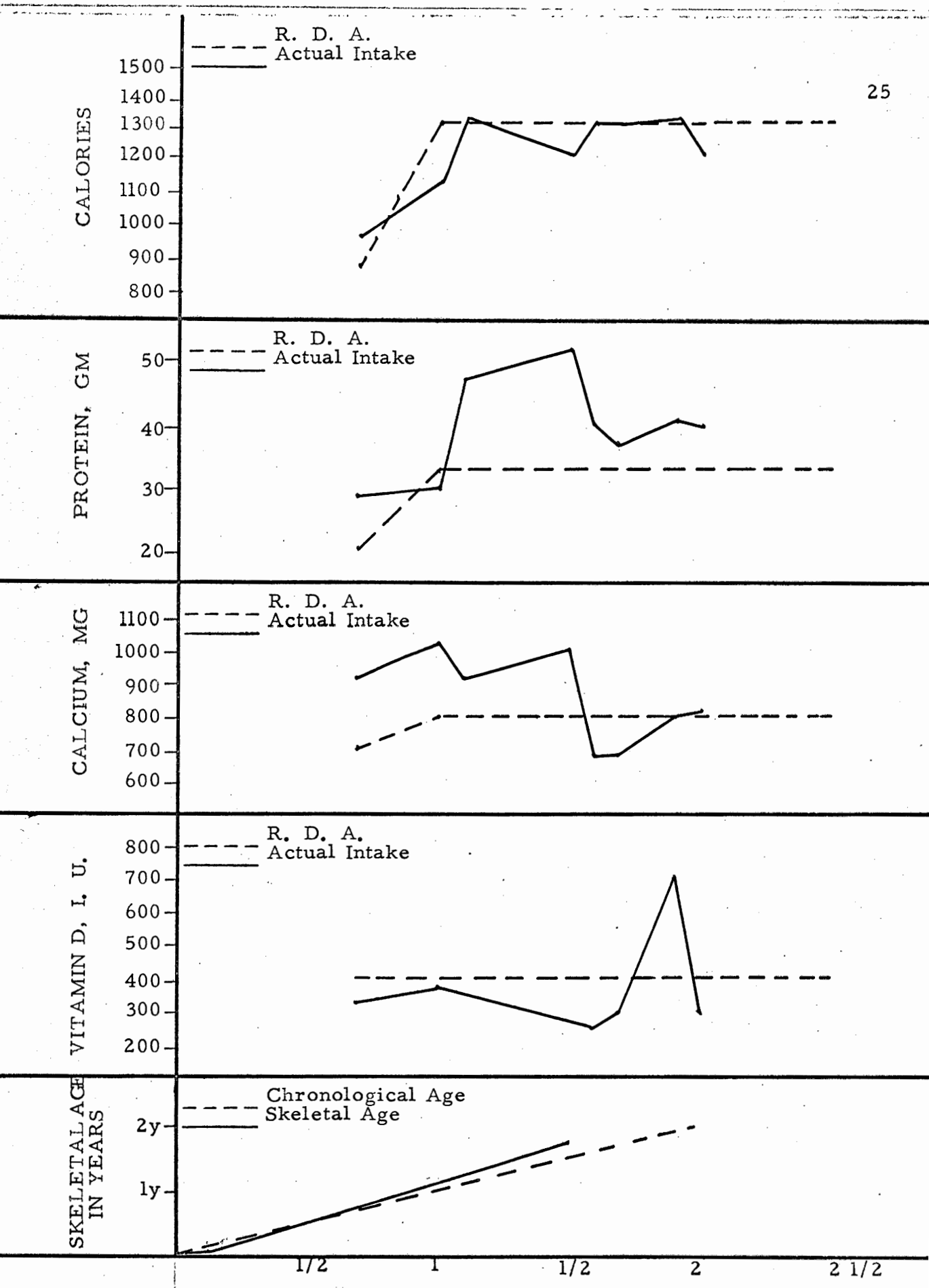

CALORIES
1500
1400
1300
1200
1100
1000
900
800
R. D. A.
Actual Intake
PROTEIN, GM
50
40
30
20
R. D. A.
Actual Intake
CALCIUM, MG
1100
1000
900
800
700
600
R. D. A.
Actual Intake
VITAMIN D, I. U.
800
700
600
500
400
300
200
R. D. A.
Actual Intake
SKELETAL AGE IN YEARS
2y
1y
Chronological Age
Skeletal Age
1/2
1
1/2
2
2 1/2

FIGURE 3

## II. CASE B

This two year old male had loss of weight after birth and was hospitalized and diagnosed at one month. He was placed on Nutramigen, had some difficulty in accepting the formula at first, but soon became adjusted to his dietary program so that by four and a half months, he was taking solids well. In fact, he appeared "always hungry" to the mother even though he was taking approximately thirty ounces of Nutramigen a day. At seven and a half months, his appetite was reported as excellent, and he was eating a variety of foods.

At the age of seven and a half months, he had cut two lower central incisor teeth and by ten months, he was walking without support. Six teeth of good quality, four upper and two lower, were visible at fourteen months. By the age of two he had seven upper teeth and eight lower teeth.

There were two bone age studies done on this child: (1) one at five and a half weeks, which demonstrated a bone age comparable with the newborn period, and (2) another study was done at one year and ten months, which reported the skeletal age to be comparable to two years. See Figure 4, page 27.

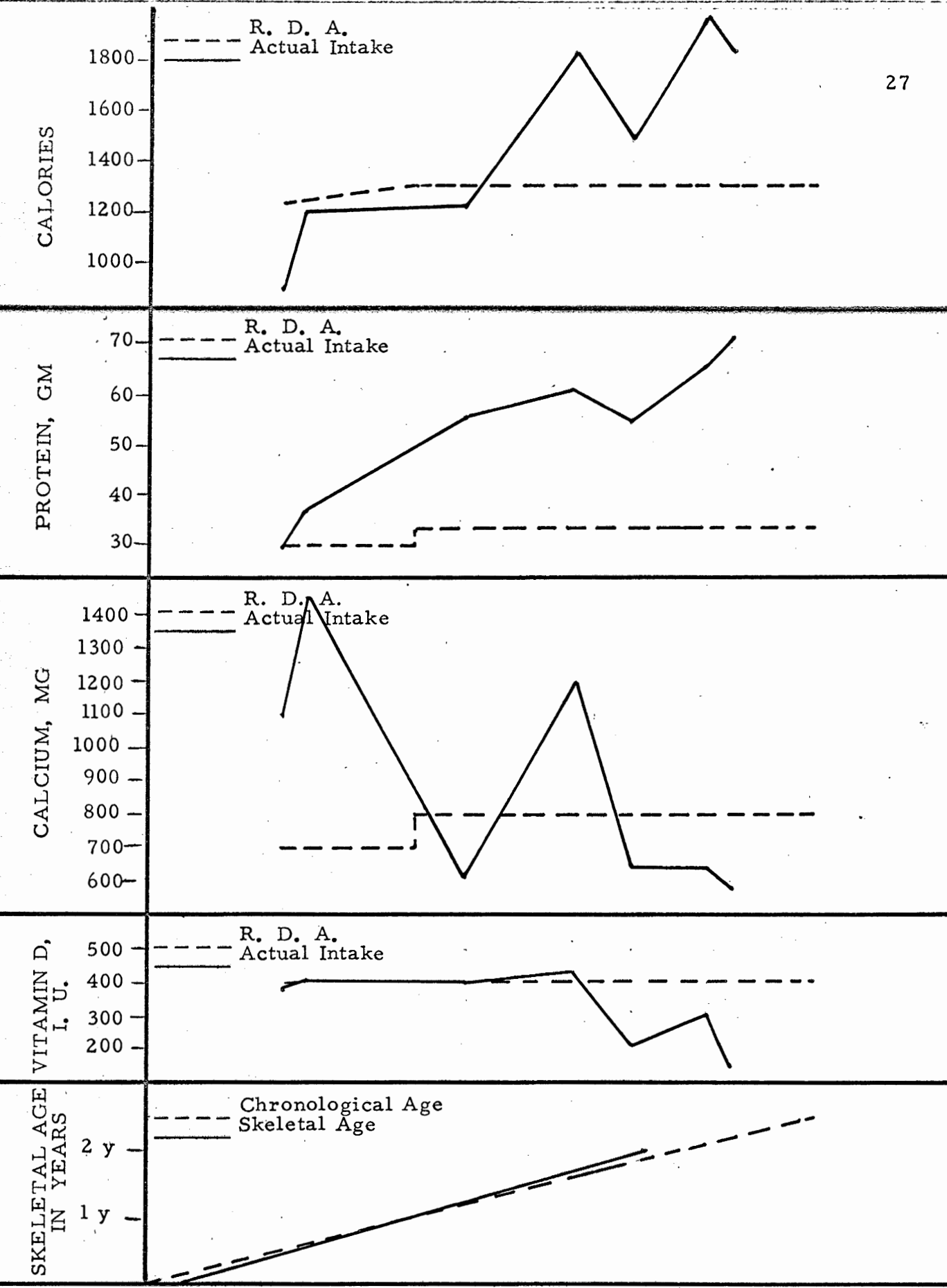



FIGURE 4

RELATIONSHIP OF SELECTED NUTRIENTS TO SKELETAL AGE OF CASE B

## III. CASE C

This six-year-old male was born in 1957 and was diagnosed at two and a half months. A soybean formula was tried after the infant seemed to resist Nutramigen, but a drop in his Developmental Quotient while on the soybean preparation prompted a return to Nutramigen. At two years of age there was still a strong resistance to Nutramigen with several breaks in the diet. The child raided the refrigerator, accepted forbidden foods from the neighbors, and was also getting peas and liver. Liver is known to contain galactose, but peas were still a questionable item at that time. By the age of three, the Nutramigen was accepted much better, but there were still intermittent breaks in the diet. Calcium tablets and vitamin tablets were added to the diet at three and a half years because of a possible calcium deficiency. The habit of "snitching" continued until after four years old, and then a report of good diet control was recorded.

Several bone ages have been done on this child. The first was at three months of age when the skeletal maturation appeared to be that of a newborn. By the age of twenty-one months, the bone age was stated to be that of approximately two years. At three, the bone age done at this time showed a skeletal age of two and a half years, which was somewhat retarded in relation to chronological age. Another study was done when the child was three years and four months old, and the report was still at the two and one half year-old range. A month before he was five years old, another bone age was done and the report showed a skeletal age of four years and six months, indicating still some slight retardation.

At twenty-one months this child had twelve teeth, and by two and a half years, he had twenty. His teeth at five years of age were reported to be of excellent quality.

## IV. CASE D

This four-year-old female was admitted to Children's Hospital when she was 12 days old with vomiting and loss of weight. She was diagnosed and started on Nutramigen at three weeks. At ten weeks, she was started on cereals, fruits, vegetables and meats, plus taking her Nutramigen. She was weaned at 14 months. When she was two years old, she drank a whole glass of milk and then vomited 4-6 ounces of it afterward. At this time, she was started on a safflower margarine. There were no more reports of dietary indiscretions. Her Nutramigen intake has been adequate throughout her history. She has been taking a vitamin preparation since she was six months old. There was no record of a calcium preparation being taken. Her appetite at three years was evidently poor as her Mother stated she had to be "coaxed" to eat.

At 16 1/2 months, this child had a dental abscess, which apparently cleared up with treatment since a report at twenty-two months was of sixteen teeth in excellent condition. However, again at two years, she was having difficulty with her teeth, as the report was that her left top molar looked inflamed. Four months later, her teeth were reported to be satisfactory. By two and a half years, her twenty teeth were in excellent condition. Another report at three years and three months gave another indication of her dental health by stating that her teeth were "beautiful".

Three bone age studies have been taken on this child. One at ten and a half months demonstrated a skeletal age of twelve months. One at sixteen and a half months reported the skeletal age within the normal range, and one at two years, which was also reported to be normal.

## V. CASE E

This male child was diagnosed at three days by a cord blood analysis. He had had a sibling diagnosed as galactosemia by autopsy findings. The mother had been kept on a low-milk diet throughout the pregnancy of this child. She had also taken a calcium supplement. This male infant was placed on Nutramigen immediately after birth.

The mother is very conscientious about the diet of this child, and has followed a rather systemized way in her feeding program with him. She gave the infant carrots at seventeen days, rice cereal at twenty-four days, bananas at twenty-four days, barley cereal at thirty-one days, beans at one and a half months, and sweet potatoes at two months. The infant also took applesauce and orange juice regularly. At the age of eight months, the baby was started on a vitamin supplement.

This child appeared well-developed and older than his age at seven months. However, a bone age taken at eight months compared closer in skeletal age to an infant three months old. This is a slight retardation, but may not persist.

## VI. CASE F

This five-year-old female was not diagnosed until she was three months old. At this time she was hospitalized for approximately ten days. Three months after her discharge from the hospital, there was reported evidence of cataracts.

This girl has apparently always been a good eater. She did well on Nutramigen and had only a few breaks in her diet. One was in chewing gum which had galactose in it and another was in eating an ice-cream sherbet which had some milk product added. After one year of age, her Nutramigen intake was low and it has been necessary since this time to supplement her diet with vitamin and mineral preparations.

At twenty months, this child had sixteen teeth of good quality. A year later, at two and a half years, her dental hygiene was excellent. At this time, however, there was a question of calcium deficiency, therefore, she was placed on a calcium supplement, Neocalglucan. Later this preparation was found to contain galactose and was substituted by calcium gluconate. At three and a half years, she broke her leg and was in a cast for four weeks. Even though she had one cavity at four years of age, her enamel and general dental health were reported to be in good shape.

This child has consistently followed a bone age comparable with her chronological age. At three months, her bone age was reported to be three months; at twenty months, reported as between eighteen months and two years; at two years and eight months, reported as approaching three years; and at three years and 10 months, reported slightly advanced at four years, and two months.

## VII. CASE $G_1$

This four-and-a-half-year-old male was diagnosed and given Nutramigen at six weeks of age. By eight months, he was taking his diet very well. This diet consisted of Nutramigen, vegetables, and fruit. It was reported that the dietary management was excellent at this time. By the age of one year, however, the Nutramigen was not accepted very well and there were several breaks in the diet. It was at this time that a report was made that the child was not only getting forbidden foods from the neighbors, but also getting liver and peas at home. A vitamin preparation was being given at this time, but no calcium supplement. When the child was eighteen months old, the mother was instructed in ways in which to increase the Nutramigen intake. Within two months, he had increased his intake from eight ounces to fourteen ounces a day. However, the protein, calories and calcium were still reported to be low. At three years of age, his protein and calorie intake had increased to above normal requirements, but the calcium intake was still slightly below the recommended amount. When the child was four years old, the mother began to add calcium and vitamin tablets to his diet, but he refused the calcium, and his calcium intake has continued to be below the recommended allowance. His diet has been reported to be lacking in vegetables and citrus fruits.

This boy's teeth have been reported to be in excellent condition. He had sixteen teeth at twenty months, and had twenty teeth with no cavities at three years and ten months.

The skeletal ages taken on this boy have all been reported to be within normal range. Four have been taken to this date. One at eight months, which showed a skeletal age of six months; one at twenty months, which reported a skeletal age of approximately two years; one at two years and six months giving a skeletal age of two years and

eight months, and one at four years and one month giving a report of over three and a half years. This case is illustrated on Figure 5, page 34.

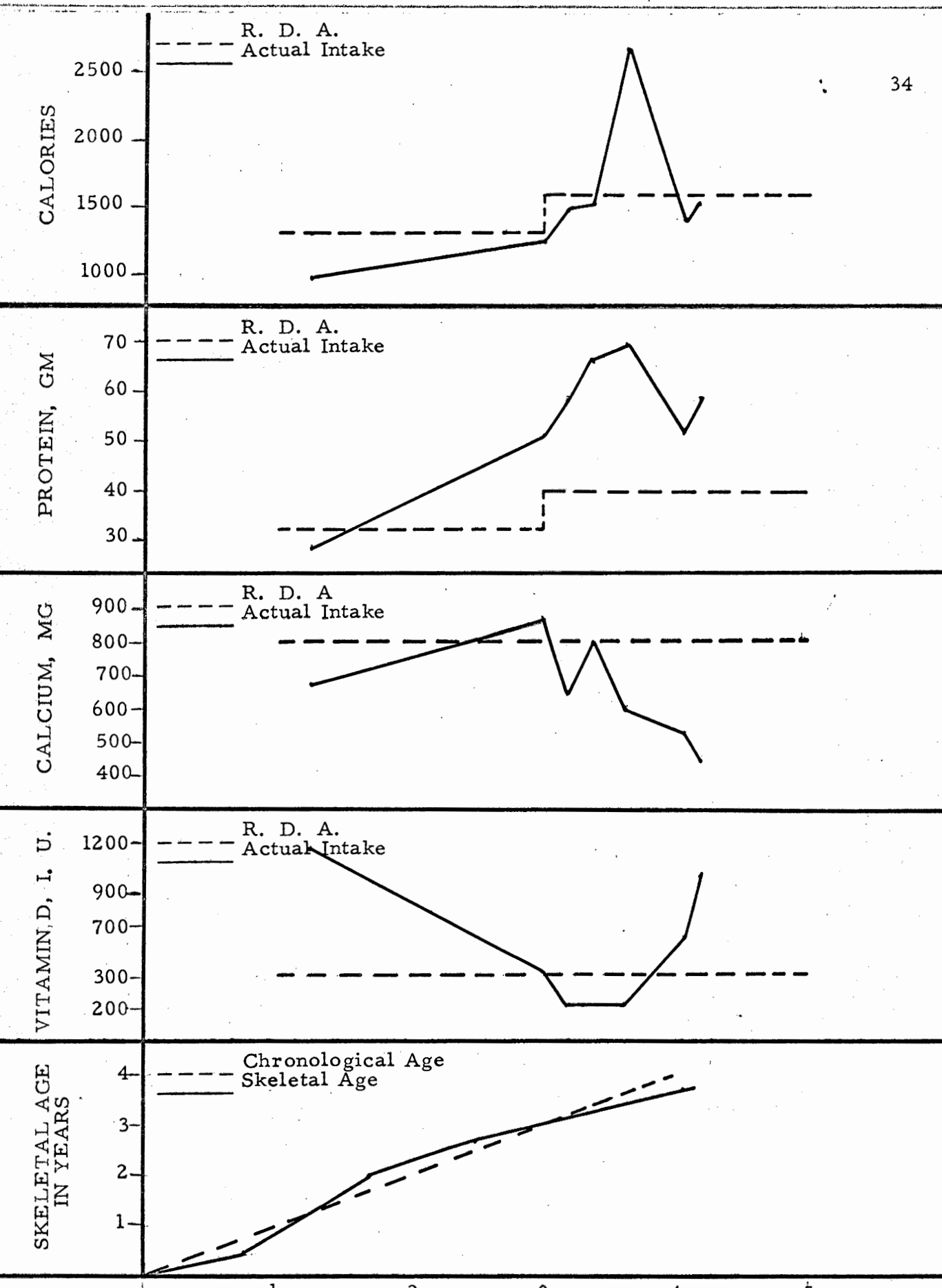

CALORIES
2500
2000
1500
1000
R. D. A.
Actual Intake
PROTEIN, GM
70
60
50
40
30
R. D. A.
Actual Intake
CALCIUM, MG
900
800
700
600
500
400
R. D. A
Actual Intake
VITAMIN D, I. U.
1200
900
700
300
200
R. D. A.
Actual Intake
SKELETAL AGE IN YEARS
4
3
2
1
Chronological Age
Skeletal Age
1
2
3
4
5

FIGURE 5

## VIII. CASE $G_2$

This two and a half year-old female, a sibling of $G_1$, was diagnosed and given Nutramigen at birth. Her Mother had drunk "gallons" of milk while pregnant with the first child, and was still taking too much milk during her pregnancy with this child. Therefore, during the third trimester, milk was eliminated from her diet and she was placed on calcium supplements. At six weeks, this infant girl was taking rice cereal, but no other solids. By four months, the mother was instructed to add yellow vegetables. The infant was taking 28 ounces of Nutramigen a day, plus rice cereal and fruit. At this time, the calcium which the infant had been taking was discontinued because of an increase in Nutramigen intake. However, a vitamin preparation was continued. At eight months, she was taking 30 ounces of Nutramigen, plus taking her solids. There was a period when her appetite was rather small, but between the ages of one and a half to two years, it changed from this rather small one to an excellent one and she also began taking more table foods. For a short while during this time, there was a discontinuance of one vitamin preparation, but by the time the child was two and a half, she was taking another type of vitamin supplement. A calcium wafer was suggested when the child was a little over two years old, but she wouldn't accept this. At this same time, she had decreased her intake of Nutramigen, so therefore her calcium intake continued to be under the recommended allowance.

This girl's dental record showed six teeth with excellent enamel at nine months. Eight central incisors, of good quality, were reported at one year of age. She had twenty teeth when she was two years old, which were reportedly in healthy condition.

Two skeletal ages have been reported on this girl. One was taken at six months and was within normal range, and one taken at two years,

which was reported as one year and three months, showing slight retardation. See Figure 6, page 37.

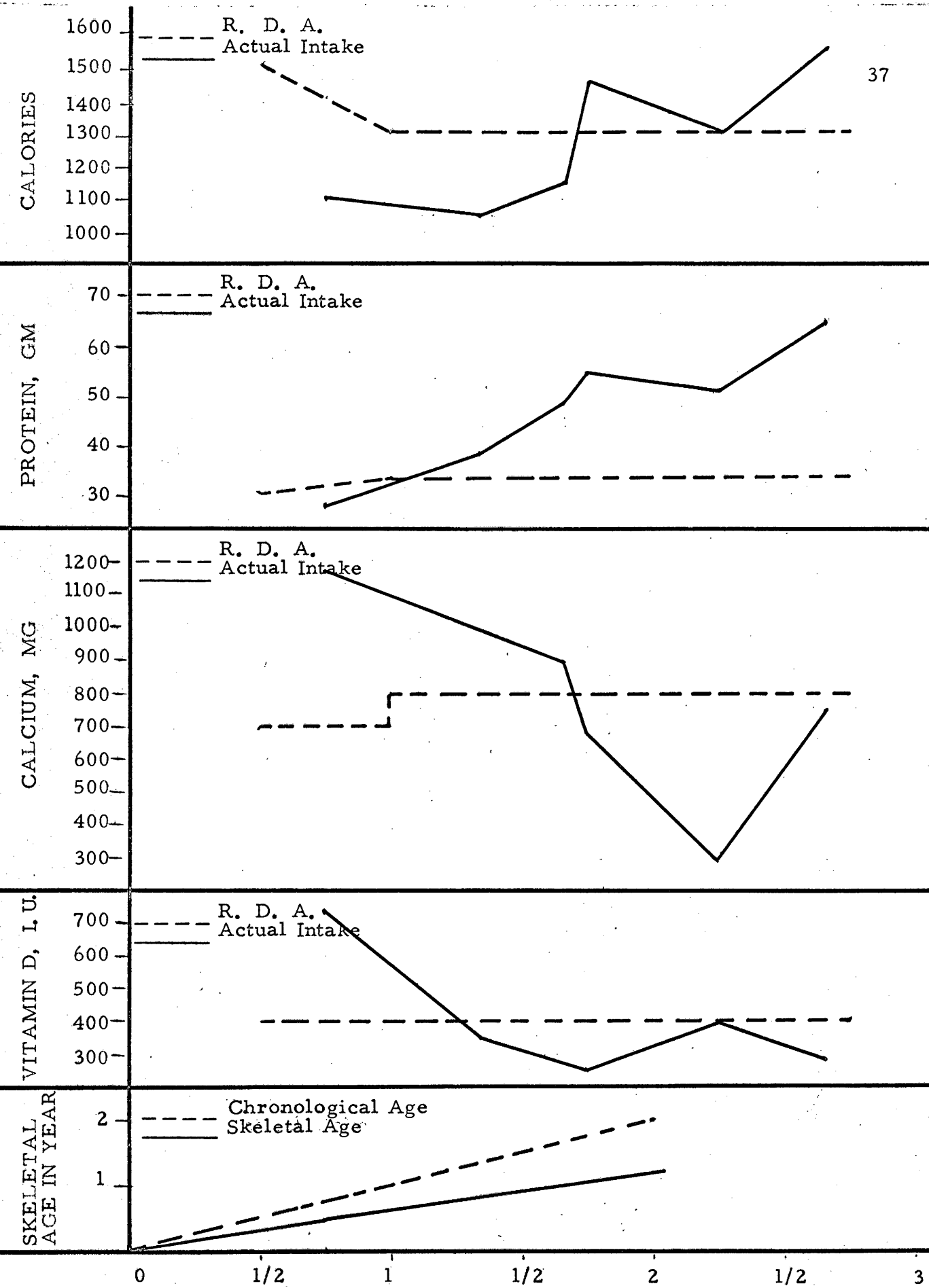



FIGURE 6
COMPARISON OF SELECTED NUTRIENTS TO SKELETAL AGE OF CASE $G_2$

## IX. CASE $H_1$

This twelve and a half year-old boy was diagnosed and started on dietary treatment at two and a half months. He has not taken Nutramigen consistently since infancy. At ten years of age, he did not drink Nutramigen, but he ate other foods well. His diet, however, was below the recommended amount in calcium, and protein. His diet did include vitamin supplements at this time, but not calcium. His Nutramigen intake improved gradually so that by the time he was eleven years old, he was taking about eighteen ounces a day. His appetite improved also, and he reportedly was taking his own lunch to school. By eleven years of age, he was meeting his nutritional needs by supplementing his diet with vitamin and mineral preparations, but it was reported that he still did not appear to be well-nourished.

The dental care on this boy was reported to be in good condition at both nine and ten years old. This indicated that his teeth were in satisfactory condition.

The first bone age recorded for this boy was at seven years of age, at which time it was reported to be between the skeletal ages of five and six, and slightly retarded. When he was ten years old, the skeletal age was determined to be that of seven years, and still retarded. Again at eleven years, the skeletal age was retarded with a reported reading between that of eight and nine years.

## X. CASE $H_2$

The sister of $H_1$ was started on Nutramigen shortly after birth because of diarrhea. Her condition immediately improved. However, she was placed back on milk at eighteen months and it wasn't until 1957, when she was five years old, that a definite diagnosis of galactosemia was established by a galactose tolerance test. She was kept on a galactose-free diet from this time on. A soybean preparation was taken until 1960, at which time Nutramigen was offered to her, but she refused to take it. Soon after this, she began to take small amounts of Nutramigen and gradually increased her intake to two cups a day. It was interesting to note that the mother had had the entire family adopt the diet of the older child, Case $H_1$, because she felt that this was easier than trying to restrict his diet alone.

This girl has been a very poor eater in the past. She was started on Nutramigen at eight years old, but it was not accepted well as stated previously. She would drink tea, coffee, and fruit juices, but very little Nutramigen. Consequently, her calories, protein and calcium intakes were below the recommended amount. By the age of ten years, her diet control was good and her Nutramigen intake had increased. She was taking vitamin and mineral supplements at this time, and at the last report, she was still continuing to take them.

This girl has had consistent bone age retardation throughout her history. At six, the first report was comparable with a standard for a three-year-old. The report at eight years showed a skeletal age of five years, and when she was nine years and four months old, her skeletal age was reported to be comparable to that of a six year-old.

## XI. CASE $I_1$

This six and a half year-old female was diagnosed at one month of age. She had been discharged from the hospital after her birth with a weight loss of 11 ounces. She was placed on Nutramigen at one month and, by three months, had gained over two pounds. By the time she was two years-old, her mother was giving her enriched bread and margarine, which contained milk products. By three and one half years, she was taking from 8 to 12 ounces of Nutramigen a day, plus taking vitamin and mineral supplements. She was getting some questionable foods in her diet at this time, but otherwise there were no other breaks in her dietary program. It was reported that the calcium preparation was not being given regularly during this time. However, in the nutritional survey of 1963-1964, it was reported that the vitamin and calcium supplements were taken every day. The Nutramigen intake has been consistently below the desired amount with this child.

This girl was the only child in this particular study who has shown dental abnormalities. By fourteen months, she had six central incisors. At one year and nine months, her ten teeth were reported to have enamel dysplasia, especially of the molars. Her teeth at two and one half years were reported of fair quality, but again at three years, there was a further report of dental dysplasia. Even though at four years, there were no cavities in her twenty teeth, the enamel dysplasia was still reported present at five years. At this same time, her teeth were described as small and stained.

The first skeletal age reported on this girl was when she was one year and nine months old. Her skeletal age was determined to be approximately twelve months. At three years of age, her skeletal age was stated to be slightly over two years. There was very little bone maturation between this time and at four years, when the bone age was reported to be approximately two and one half years. When she was five years and

eight months old, her skeletal age was reported to be that of three years and six months, which showed considerable bone retardation.

## XII. CASE $I_2$

A sibling of $I_1$, this three-year-old male was diagnosed by a cord blood analysis and started on Nutramigen at birth. Soon after this, at three weeks, he was placed on a meat-base formula and has continued on this. At five months, his intake of this formula was 32 ounces each day. He was also taking additional solids, such as fruits, cereals, meat and vegetables. His intake of the meat-base formula was excellent at one year, at which time he was also taking a vitamin supplement. There was a slight possibility of calcium deficiency noted at this time, so therefore, he was placed on calcium supplements, also. By the age of two years, he had decreased his intake of the formula to 1 1/2 cups a day. During the nutritional survey of 1963-1964, he has reportedly taken the vitamin and calcium supplements consistently.

This boy's dental reports show that he had six teeth, of good quality, at ten and a half months. At fourteen and a half months, he had eight teeth, which demonstrated good calcification. By the age of eighteen months, his sixteen teeth were reported to be of good quality.

The only skeletal age recorded so far on this child was at ten and a half months. This was determined to be approximately fifteen months, which was slightly advanced for his chronological age.

# CHAPTER V

## RESULTS AND DISCUSSION

The data can be classified under three categories: selected nutritional factors, skeletal age and other determinations. The average value for the selected nutrients for each child was determined from all the available data; however, in most cases this nutritional data could not be correlated with the skeletal age because of the wide variance in time of recording the two. Therefore, only four of the studies were used to determine a correlation. These four are graphically portrayed in Figures 2 through 5 on pages 25, 27, 34 and 37. It should be pointed out that all of these four children were under five years of age. A summary of the selected nutritional factors, bone ages, and other determinations of all the children in the study is found in Table I on pages 44 through 46.

### I. SELECTED NUTRITIONAL FACTORS

Calories. On the whole, the calories consumed fell within the Recommended Allowance, however, there were two of the children who had caloric values in the diet low enough to be considered a therapeutic problem. These two were Cases F and 4. The latter has retardation of bone growth.

Protein. With the exception of Case E, all the children consumed more than the Recommended Allowance of Protein. His skeletal age is slightly retarded; however, a longer study would be necessary to assume a correlation in this factor.

Calcium. Seven of the children in this study showed an intake of calcium less than the Recommended Allowance, and of these seven, three had some degree of bone retardation. However, in view of the many variables throughout the study, it is difficult to make a corre-

## SUMMARY OF SELECTED HISTORICAL DATA OF TWELVE GALACTOSEMIC CHILDREN

### TABLE I

| Case & Sex | Birth-date | Age At Diagnosis | Age When Dietary Treatment Started | Dental Reports | Skeletal Age Reports | Average Nutritional Status of Selected Factors as % of R. D. A.* |
|---|---|---|---|---|---|---|
| A FEMALE | 2-15 1962 | 2 weeks | 2 weeks | Good | Normal | Calories - 97%<br>Protein - 129%<br>Calcium - 110%<br>Vitamin D - 95% |
| B MALE | 1-4 1962 | 1 month | 1 month | Good | Normal | Calories - 115%<br>Protein - 165%<br>Calcium - 120%<br>Vitamin D - 85% |
| C MALE | 9-20 1957 | 2 1/2 months | 2 1/2 months | Excellent | Slight Retardation | Calories - 98%<br>Protein - 109%<br>Calcium - 103%<br>Vitamin D - 182% |
| D FEMALE | 2-27 1960 | 3 weeks | 3 weeks | Excellent | Normal | Calories - 101%<br>Protein - 142%<br>Calcium - 132%<br>Vitamin D - 205% |

* Recommended Daily Allowance

TABLE I
(continued)

| Case & Sex | Birth-date | Age At Diagnosis | Age When Dietary Treatment Started | Dental Reports | Skeletal Age Reports | Average Nutritional Status of Selected Factors as % of R. D. A.* |
|---|---|---|---|---|---|---|
| E MALE | 5-9 1963 | Birth | Birth | No Report | Slight Retardation | Calories - 111%<br>Protein - 74%<br>Calcium - 111%<br>Vitamin D - 132% |
| F FEMALE | 8-5 1958 | 3 months | 3 months | Excellent | Normal | Calories - 86%<br>Protein - 168%<br>Calcium - 97%<br>Vitamin D - 181% |
| $G_1$ MALE | 7-28 1959 | 6 weeks | 6 weeks | Excellent | Normal | Calories - 105%<br>Protein - 141%<br>Calcium - 82%<br>Vitamin D - 150% |
| $G_2$ FEMALE | 5-15 1961 | Birth | Birth | Excellent | Normal | Calories - 96%<br>Protein - 148%<br>Calcium - 92%<br>Vitamin D - 100% |

TABLE I
(continued)

| Case & Sex | Birth-date | Age At Diagnosis | Age When Dietary Treatment Started | Dental Reports | Skeletal Age Reports | Average Nutritional Status of Selected Factors as % of R. D. A. * |
|---|---|---|---|---|---|---|
| $H_1$ MALE | 3-31 1951 | 2 1/2 months | 2 1/2 months | Good | Retardation | Calories - 106%<br>Protein - 124%<br>Calcium - 74%<br>Vitamin D - 207% |
| $H_2$ FEMALE | 9-24 1952 | five years | 2 weeks | None recorded | Retardation | Calories - 100%<br>Protein - 147%<br>Calcium - 83%<br>Vitamin D - 185% |
| $I_1$ FEMALE | 9-27 1957 | 1 month | 1 month | Enamel dysplasia | Retardation | Calories - 89%<br>Protein - 113%<br>Calcium - 61%<br>Vitamin D - 117% |
| $I_2$ MALE | 4-17 1961 | Birth | Birth | Good | Slightly Advanced | Calories - 108%<br>Protein - 128%<br>Calcium - 72%<br>Vitamin D - 103% |

lation of this result. For instance, one of the children having an intake less than recommended had a skeletal age slightly in advance of his chronological age; and another child who had an 82% intake of calcium in comparison with the Recommended Allowance had a skeletal age comparable to his chronological age. Two with normal skeletal age had low intakes of calcium but were above 90% and therefore not considered significant. This is illustrated in Figure 5, page 33.

Vitamin D. Only one of the children, Case B., Figure 4, page 27, had a Vitamin D intake which could be considered below the Recommended allowance. This child was above the average in his consumption of all the other selected nutrients in the study. The skeletal age on this child was within the normal range; therefore, it would be difficult to attempt a correlation in this case.

## II. SKELETAL AGE

Skeletal Age. Averages for the nutritional status of each child were taken in order to determine a correlation of skeletal age with selected nutrients. There are many variables in attempting to correlate any factor with the skeletal age of a child. An illness may interfere with normal ossification and thereby cause some retardation in the skeletal growth of the child. (36) Because of this, plus the variables in the dietary analyses, it would be ineffectual to attempt a correlation. It was interesting to note that three out of seven of the children who had an intake below the Recommended Allowance of calcium had bone retardation. There is however, an indication that optimum nutrition itself is a safeguard against not only retardation in bone growth, but also against the illness that may interfere with this growth. (36)

## III. OTHER DETERMINATIONS

Age of Diagnosis. In view of the complications of the untreated galactosemic child, the age at when the diagnosis was confirmed could present a variable in attempting to correlate skeletal age with any other factor. As seen from Table I, pages 44 through 46, three of the children in this study were diagnosed at birth, and of these three, one, Case E, had slight bone retardation, one, Case $I_2$, had slightly advanced skeletal age and one, Case $G_2$, had a skeletal age comparable with the chronological age.

Of the children studied who had been diagnosed within the first month of life, three were normal in their skeletal age and one had bone retardation. As illustrated in Table I, pages 44 through 46, Case A, B, and D were all normal in skeletal age and Case $I_1$ had bone retardation.

Of the five children who were diagnosed after the first month of life, three showed some degree of bone retardation. It was not determined if the degree of bone retardation corresponded to the length of time which had elapsed before diagnosis had been confirmed.

Age When Dietary Treatment Started. Most of the children started on the dietary treatment at the time of diagnosis; however, this could be a determining factor and should be considered. One child, Case $H_2$, was not definitely diagnosed until she was five years old, nevertheless, she had been on a restricted galactose diet since two weeks of age.

Because of the many variables which had to be taken into consideration, no definite conclusions can be drawn from this study as to the effects of the nutritional status on the skeletal age of a child with galactosemia.

# CHAPTER VI

## SUMMARY, CONCLUSIONS, AND RECOMMENDATIONS

Twelve children with galactosemia, ranging in ages from three months to twelve years of age, were selected for a pilot study to determine if a correlation existed between the nutritional intake of calories, protein, calcium and Vitamin D and the skeletal age. These selected nutrients were analyzed and compared with the Recommended Daily Allowances as revised in 1963.

Prior to, and during the study, the skeletal ages were determined by radiological reports. These roentgenographs are made only once a year on each child in the Child Development Clinic.

The percentage of nutritional history forms which were completed and returned by the parents was sufficient for determining the average intake of the selected nutrients, but there was such a large lapse in time between the collection of nutritional data and the skeletal age reports that a correlation between these two factors was not possible in all cases. Only in four out of the twelve cases presented in this study could a correlation be demonstrated in a graphic form. This is one-third of the total number studied, and does not serve as a valid representation. Consequently, there was no definite relationship between the nutritional status of galactosemic children and their skeletal ages.

The need for including the nutritionist as a member of the multi-disciplinary team cannot be over emphasized. In a disease such as galactosemia in which the only treatment is a dietary one, a nutritionist is of invaluable help.

Based on the results obtained from this study, several recommendations are made for further research. One of the largest variables could be removed by having a three-day nutritional history form mailed to the parents. These could be completed prior to the next

visit to the clinic, and could be brought to the clinic and given to the nutritionist. At the time of the visit, the completed 3-day nutritional history could be reviewed with the nutritionist so that all vitamin and mineral preparations could be included. If a visit is made to the clinic only once a year, the nutritionist should mail at least two other history forms during the remainder of the year. This would assure a more valid interpretation of the dietary intake. The importance of completing these forms should be stressed to the parent.

Another variable could be removed by encouraging the parents to be consistent in recording the vitamin and mineral supplements in the child's diet. These preparations may make the difference between a diet which is low in nutrients and one which is high.

A variable which will need to be removed before further dietary evaluations can be made is the standardization of the nutrients contained in the various vitamin and mineral preparations. The pharmaceutical companies should be contacted in order to obtain the specified amount of each nutrient in their product. Most of the companies vary in manner in which the ingredients are listed on the label, and this makes it very difficult to know the exact amount contained in the preparation.

The ideal, of course, would be to have the nutritionist visit the home of each child periodically to answer questions about the diet, and to evaluate the dietary intake in the home environment. A much closer relationship between the nutritionist and the parents could be established in this way, and by this, could encourage a more meaningful evaluation.

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# APPENDIX

**Foods which may be included and should be excluded in a galactose-free diet**

| FOODS INCLUDED | FOODS EXCLUDED* |
|---|---|
| **Milk and Milk Products** | |
| None; Nutramigen and soybean milks used as milk substitutes | all milk of any species and all products containing milk, as skim, dried, evaporated, condensed; yogurt; cheese; ice cream; sherbet; malted milk |
| **Legumes** | |
| All may be included if facilities are available for monitoring erythrocyte galactose-1-phosphate | |
| **Meat, Fish, and Fowl** | |
| Plain beef, chicken, fish, turkey, lamb, veal, pork, and ham | creamed or breaded meat, fish, or fowl; sausage products, such as wieners, liver sausage, cold cuts containing milk; organ meats, such as liver, pancreas, and brain |
| **Eggs** | |
| All | none |
| **Vegetables** | |
| Artichokes, asparagus, beets, broccoli, cabbage, carrots, cauliflower, celery, chard, corn, cucumber, eggplant, green beans, kale, lettuce, mustard, okra, onions, parsley, parsnips, pumpkin, rutabagas, spinach, squash, tomatoes | sugar beets, peas, Lima beans; creamed, breaded, or buttered vegetables; canned or frozen vegetables, or corn curls if lactose is added during processing |
| **Potatoes and Substitutes** | |
| White and sweet potatoes, yams, macaroni, noodles, spaghetti, rice | any creamed, breaded, or buttered; French fried or instant potatoes if lactose is added during processing |
| **Breads and Cereals** | |
| Any that do not contain milk or milk products† | prepared mixes, such as muffins, biscuits, waffles, pancakes; some dry cereals; Instant Cream of Wheat. *Read labels carefully.* |
| **Fats** | |
| Margarines‡ and dressings which do not contain milk or milk products; oils; shortenings; bacon | margarines and dressings containing milk or milk products; butter; cream; cream cheese |
| **Soups** | |
| Clear soups; vegetable soups which do not contain peas or Lima beans; consommés | cream soups, chowders, commercially prepared soups containing lactose |
| **Desserts** | |
| Water and fruit ices; gelatin; angel food cake; homemade cakes, pies, cookies made from acceptable ingredients | commercial cakes and cookies and mixes; custard, puddings, ice cream made with milk; any containing chocolate |
| **Fruits** | |
| All fresh; canned or frozen that are not processed with lactose | any canned or frozen processed with lactose |
| **Miscellaneous** | |
| Nuts and nut butters, unsalted popcorn, olives, pure sugar candy, jelly or marmalade, sugar, corn sirup | gravy, white sauce, chocolate, cocoa, toffee, peppermints, butterscotch, caramels, molasses, candies, instant coffee, powdered soft drinks, monosodium glutamate, some spice blends, chewing gum |

*In all instances, labels should be read carefully and any product which contains milk, lactose, casein, whey, dry milk solids, or curds should be omitted.

†In each area, bakeries should be contacted and a list of acceptable products made available.

‡In the Los Angeles area: Mother's, Hollywood.

# THREE-DAY NUTRITIONAL HISTORY FORM

## DIRECTIONS FOR RECORDING

When recording what your child has eaten, this list may be helpful.

Liquid in cups or ounces.

Vegetables, cereals and fruits in tablespoons or a portion of a cup.

Strained or chopped meat in tablespoons or a portion of a cup.

Other meat in approximate ounces or pieces.

Eggs - list number.

Bread in number of slices (if a spread is used, be sure to record. If margarine, please list the kind.)

Mixed dishes in portion of a cup. Also list the ingredients as in casserole or salad or dessert.

Pudding - (list kind) in a portion of a cup.

Example:

| | |
|---|---|
| 1 Hamburger | 2 ounces |
| Green Beans | 1/2 cup |
| Homemade bread with grape jelly | 1/2 slice |
| Applesauce | 1/2 cup |
| Orange | 4 ounces (small juice glass) |

If your child is taking any vitamins or medication, please record the kind and amount for each day.

NAME _____ AGE _____ DATE _____

| | |
|---|---|
| BREAKFAST | |
| BETWEEN BREAKFAST AND LUNCH | |
| LUNCH | |
| BETWEEN LUNCH AND SUPPER | |
| SUPPER | |
| AFTER SUPPER | |

LOMA LINDA UNIVERSITY
SCHOOL OF GRADUATE STUDIES

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# A Pilot Study of the Relation of Selected Nutritional Factors to Skeletal Age of Galactosemic Children

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by

Jessie Merle Harper

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An Abstract of a Thesis
of the Requirements for the Degree
Master of Science in the Field of Nutrition

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June, 1964

## ABSTRACT

A pilot study was conducted in which twelve children with galactosemia were selected to determine if a correlation existed between the dietary intake of calories, protein, calcium and vitamin D, and the skeletal age of each child. The selected nutrients were compared with the Recommended Daily Allowances as revised in 1963. The skeletal ages were determined by the standards as established by Greulich and Pyle. (36).

The medical records of these twelve galactosemic children were studied for previous data pertinent to their growth and development. The data which were especially emphasized were: nutritional information and skeletal radiological reports. To receive more information on the nutritional intake of calories, protein, calcium and vitamin D, a 3-day nutritional history form was mailed to the parent of each child once a month for a period of six months.

Because of the large lapse in time between the collection of nutritional data and the skeletal age reports, a correlation between these two factors was not possible in all cases. Of the twelve children selected for the study, only four could be used to determine a graphic correlation. Consequently, in this study, there was no definite correlation seen between the nutritional status of galactosemic children and their skeletal age.

It was concluded that based on results obtained, investigation should be continued before significant statements could be made.